Docket No.: 3893-0200PUS2
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Tore DUVOLD

Application No.: NEW | Confirmation No.:

Filed: October 4, 2004 | Art Unit: N/A

For: BRANCHED POLYAMINE STEROID DERIVATIVES | Examiner: Not Yet Assigned

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The PTO is requested to use the amended sheets/claims attached hereto (which correspond to Article 19 amendments or to claims attached to the International Preliminary Examination Report (Article 34) during prosecution of the above-identified national phase PCT application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: October 4, 2004
ADM/nl

Respectfully submitted,

By _____
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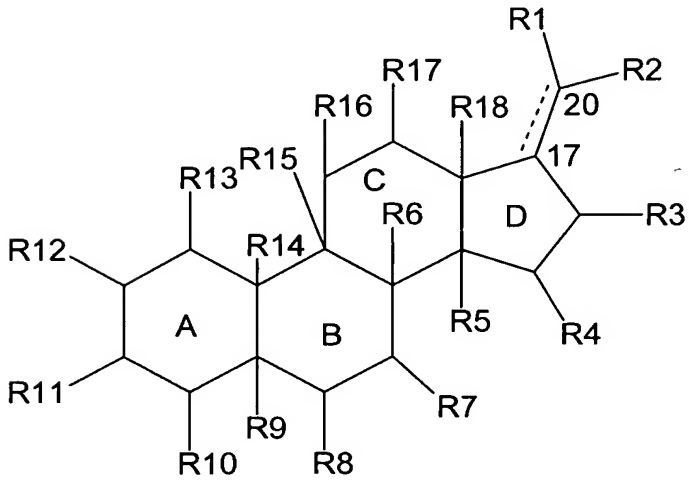
CLAIMS

1. A compound according to formula I



I

wherein the fused rings A, B, C and D are independently saturated or fully or partially unsaturated;

the bond between C-17 and C-20 is depicted with a full and a dotted line to indicate that said bond can be a single or a double bond;

wherein R1 is hydrogen, halogen, a lipophilic group, $-(Z)_n-(NR-Z)_p-N(R)_2$ or $C(O)-(Z)_n-(NR-Z)_p-N(R)_2$, wherein n is 0 or 1 and p is an integer from 1 and 5;

each Z independently represents straight or branched hydrocarbon diradical, optionally substituted with C_{1-6} alkyl, C_{1-6}alkenyl, C_{1-6}alkynyl, hydroxy, alkoxy, amino, C_{1-6}aminoalkoxy, C_{1-6}aminoalkyl, C_{1-6}aminoalkylaminocarbonyl, C_{1-6}alkylC_{3-8}cycloalkyl or C_{1-6}alkylheteroaryl;

each R independently represents hydrogen or C_{1-6}alkyl, C_{1-6}aminoalkyl, C_{1-6}aminoalkoxy or C_{1-6}aminoalkylaminocarbonyl, all of which are optionally substituted with alkyl or C_{1-6}aminoalkyl;

provided that at least one Z is substituted with C_{1-6} alkyl, C_{1-6}alkenyl, C_{1-6}alkynyl, hydroxy, alkoxy, C_{1-6}aminoalkoxy, C_{1-6}aminoalkyl, C_{1-6}aminoalkylaminocarbonyl, C_{1-6}alkylC_{3-8}cycloalkyl or C_{1-6}alkylheteroaryl, or at least one R is different from hydrogen;

R2 represents halogen, C_{1-4}alkyl, optionally substituted with COOH; C_{1-4}alkoxy, -COOH, $-(Z)_n-(NR-Z)_p-N(R)_2$ or $C(O)-(Z)_n-(NR-Z)_p-N(R)_2$;

R3 represents hydrogen halogen or O-R19, wherein R19 represents hydrogen, $-SO_3$, C_{1-6}alkyl, C_{1-6}acyl or $-(Z)_n-(NR-Z)_p-N(R)_2$;

each of R4, R7, R8, R10, R11, R12, R13, R16 and R17 independently represent hydrogen, halogen, hydroxy, $-OSO_3$, -O-acyl, $-(Z)_n-(NR-Z)_p-N(R)_2$ or

Replaced by Art. 19.

$C(O)-(Z)_n-(NR-Z)_p-N(R)_2$;
each of R5, R6, R9, R14, R15 and R18 independently represent hydrogen or methyl or are each independently absent when one of the fused rings, A, B, C and D are unsaturated so as to complete the valency of the carbon atom at that site;
provided that at least one, and not more than three of R1, R2, R4, R7, R8, R10, R11, R12, R13, R16 and R17 is $-(Z)_n-(NR-Z)_p-N(R)_2$ or
$C(O)-(Z)_n-(NR-Z)_p-N(R)_2$;
and pharmaceutically acceptable salts or esters thereof.

2. A compound according to claim 1, wherein R2 represents $-(Z)_n-(NR-Z)_p-N(R)_2$ or $C(O)-(Z)_n-(NR-Z)_p-N(R)_2$.

3. A compound according to claim 1, wherein R7, R11 and/or R16 represents $-(Z)_n-(NR-Z)_p-N(R)_2$ or $C(O)-(Z)_n-(NR-Z)_p-N(R)_2$.

4. A compound according to claim 1, wherein R1 represents a lipophilic group.

5. A compound according to claim 1, wherein R1 is selected from the group consisting of straight or branched, saturated or unsaturated C_{1-10}alkyl, aryl, C_{3-8}cycloalkyl, aralkyl with 1-10 carbon atoms in the alkyl moiety, C_{1-10}alkylaryl, C_{1-10}alkyl-C_{3-8}cycloalkyl, C_{1-10}alkoxy and heteroaryl.

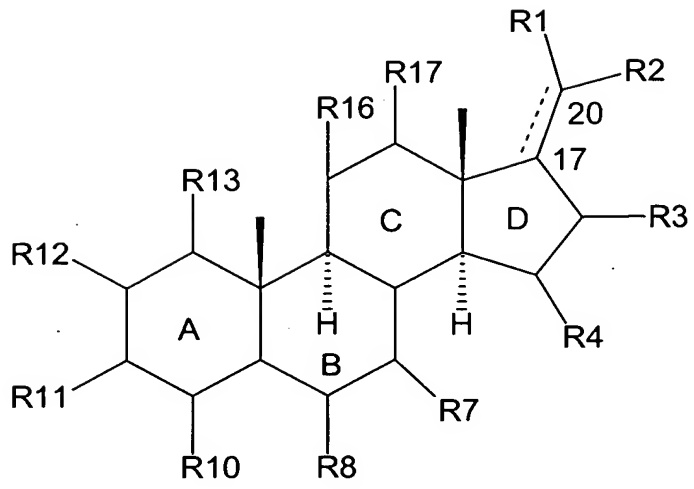
6. A compound according to any of claims 1-5, wherein R19 represents C_{1-6}alkyl or C_{1-6}acyl.

7. A compound according to any of claims 1-6, wherein R7, R11 and/or R16 represent OH

8. A compound according to any of claims 1-5, wherein R11 represents $-OSO_3$.

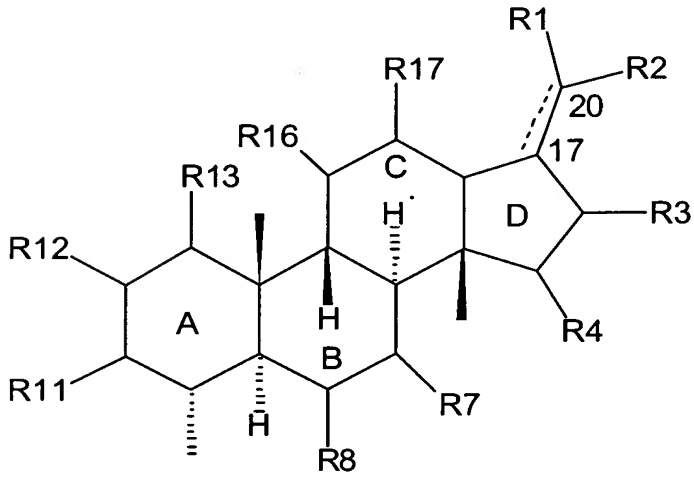
9. A compound according to any of claims 1-5, wherein R11 represents –O-acyl.

10. A compound according to any of claims 1 which has the general formula Ia



Ia

11. A compound according to any of claims 1 which has the general formula Ib



Ib

12. A compound according to claim 10 or 11, wherein R2 represents $-(Z)_n-(NR-Z)_p-N(R)_2$ or $C(O)-(Z)_n-(NR-Z)_p-N(R)_2$.

13. A compound according to claim 12, wherein R7 and R11 are both hydroxy.

14. A compound according to claim 12, wherein R11 and R16 are both hydroxy.

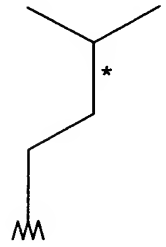
15. A compound according to claim 12, wherein R3 is –OR19, wherein R19 is C_{1-6}alkyl or C_{1-6}acyl.

Replaced by Art. 19

16. A compound according to claim 12, wherein R1 is a lipophilic group.

17. A compound according to claim 12, wherein R1 is a straight or branched, saturated or unsaturated C_{1-10}hydrocarbon.

18. A compound according to claim 12, wherein R1 is a moiety of formula II



II

wherein the carbon-carbon bond denoted "*" is a single or double bond.

19. A compound according to claims 10 or 11, wherein R11 represents $-(Z)_n-(NR-Z)_p-N(R)_2$ or $C(O)-(Z)_n-(NR-Z)_p-N(R)_2$.

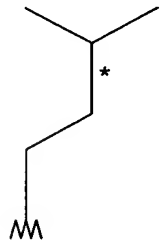
20. A compound according to claim 19, wherein R2 is C_{1-4}alkyl, optionally substituted with COOH, C_{1-4}alkoxy or COOH.

21. A compound according to claim 19, wherein R3 is O-R19, wherein R19 represents C_{1-6}alkyl or C_{1-6}acyl.

22. A compound according to claim 19, wherein R1 is a lipophilic group.

23. A compound according to claim 19, wherein R1 is a straight or branched, saturated or unsaturated C_{1-10}hydrocarbon.

24. A compound according to claim 19, wherein R1 is a moiety of formula II



II

wherein the carbon-carbon bond denoted "*" is a single or double bond.

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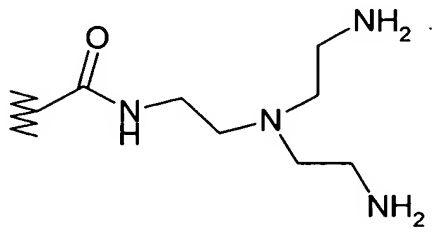
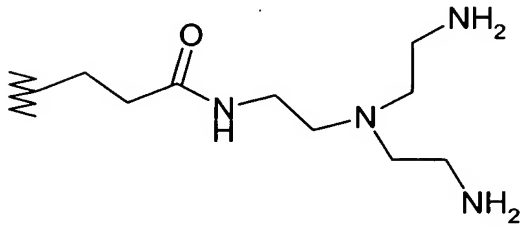
25. A compound according to any one of claims 1, 10 or 11, wherein R2 and/or R11 represents a moiety of the formula VIII, IX, X, XI, XII, XIII, XVI, XVII, XVIII, XIX, XX, XXI, XXII, XXIII



VIII



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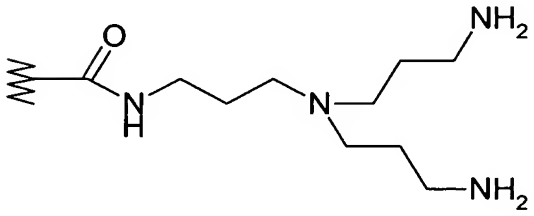
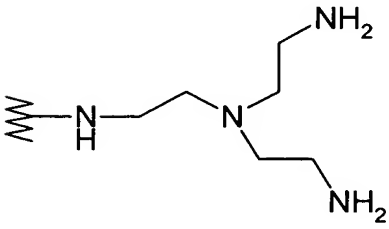


X



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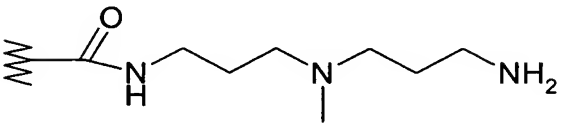

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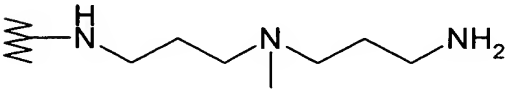

XIII

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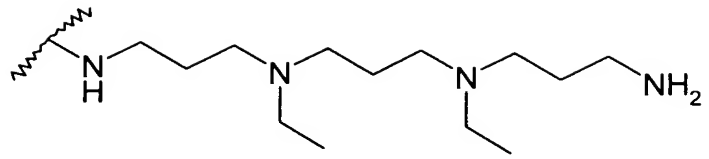
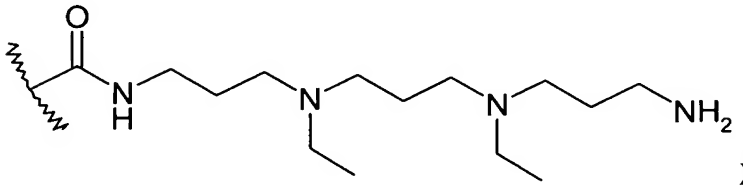


XVI



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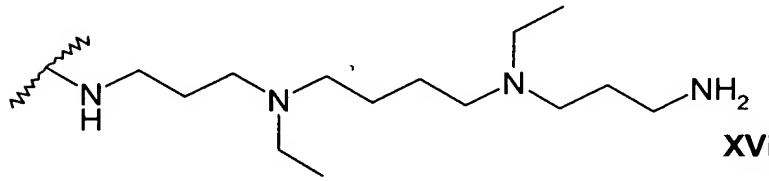
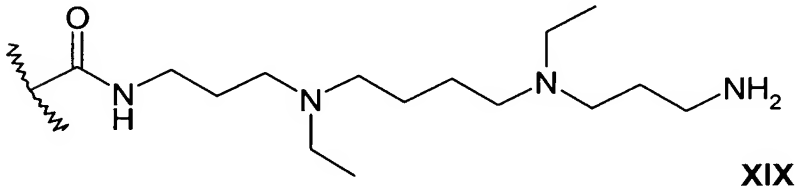
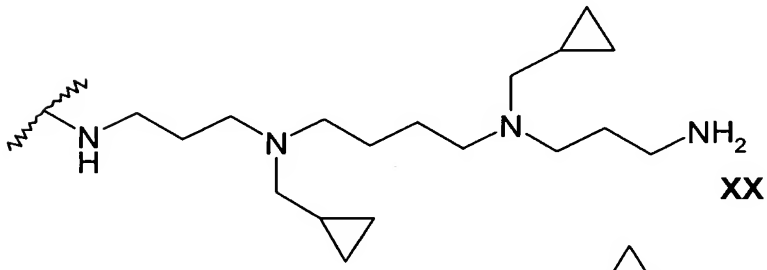


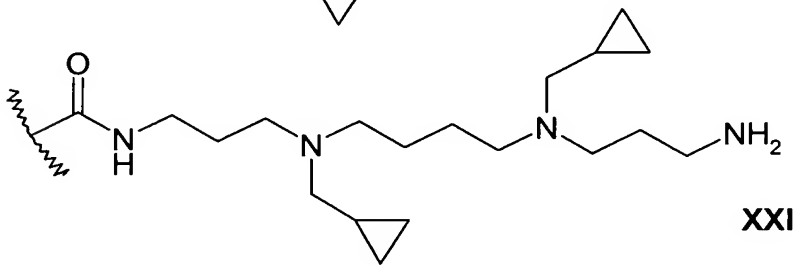
XVIII



XIX



XX



XXI

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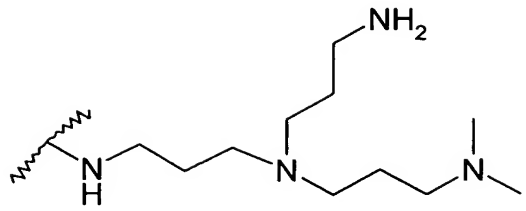
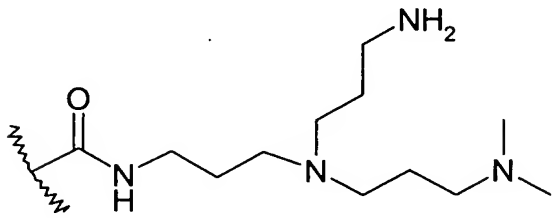


XXII



XXIII

26. A compound according to claim 1 selected from the group consisting of

21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-17R,20S,24,25-tetrahydrofusid-21-amide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-11-desoxy -17R,20S,24,25-tetrahydrofusid-21-amide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-16-desacetoxy-17R,20S,24,25-tetrahydrofusid-21-amide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-13(17)-en-17,20,24,25-tetrahydrofusidan-21-carboxamide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-3β- desacetoxy-17R,20S,24,25-tetrahydrofusid-21-amide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-9(11)-en-17R,20S,24,25-tetrahydrofusid-21-amide,
24-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-3α-hydroxy-5β-cholan-24-amide,
22- N-{2'-[bis(2'-aminoethyl)amino]ethyl}-23,24-bisnor-5-cholenic-22-amide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-fusid-21-amide,
21-N-{3'-[bis(3'-aminopropyl)amino]propyl}-fusid-21-amide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-3-OSO_3-11-desoxy-17,20,24,25-tetrahydro-fusid-21-amide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-11-desoxy-16-desacetoxy-17S,20,24,25-tetrahydrofusid-21-amide,
21-N-{3'-[bis(3'-aminopropyl)amino]propyl}-17R,20S,24,25-tetrahydrofusid-21-amide,
22-N-{3'-[bis(3'-aminopropyl)amino]propyl}-23,24-bisnor-5-cholenic-22-amide,
21-N-{3'-[bis(3'-aminopropyl)amino]propyl}-}-3-OAc-17R,20S,24,25-tetrahydrofusid-21-amide,

21-N-{3'-[bis(3'-aminopropyl)amino]propyl}-}-3-OSO_3-11-desoxy-17,20,24,25-tetrahydrofusid-21-amide,
21-N-{3'-[bis(3'-aminopropyl)amino]propyl}-}-11-desoxy-16-desacetoxy-17S,20,24,25-tetrahydrofusid-21-amide,
3-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-fusidic acid,
21-N-{3'-[(3'-aminopropyl)(methyl)amino]propyl}-17R,20S,24,25-tetrahydrofusid-21-amide,
21-N-{3'-[(3'-aminopropyl)(methyl)amino]propyl}-11-desoxy-17R,20S,24,25-tetrahydrofusid-21-amide,
21-N-{3'-[(3'-aminopropyl)(methyl)amino]propyl}-16-desacetoxy-17R,20S,24,25-tetrahydrofusid-21-amide,
24-N-{3'-[(3'-aminopropyl)(methyl)amino]propyl -3α-hydroxy-5β-cholan-24-amide,
21-N-{3'-[(3'-aminopropyl)(methyl)amino]propyl}-11desoxy-16-desacetoxy-17R,20S,24,25-tetrahydrofusid-21-amide,
3-N-{3'-[bis(3'-aminopropyl)amino]propyl}-}-fusidic acid,
3-N-{3'-[(3'-aminopropyl)(methyl)amino]propyl}-fusidic acid,
21-N-{3-({4'-[(3'-amino-propyl)-methyl-amino]-butyl}-methyl-amino)-propyl}-17R,20S,24,25-tetrahydrofusid-21-amide,
21-N-{3'-({3'-[(3'-amino-propyl)-ethyl-amino]-propyl}-ethyl-amino)-propyl}-17R,20S,24,25-tetrahydrofusid-21-amide,
21-N-{3'-({4'-[(3'-amino-propyl)-ethyl-amino]-butyl}-ethyl-amino)-propyl}-17R,20S,24,25-tetrahydrofusid-21-amide,
21-N-{3-({3'-[(3'-amino-propyl)-ethyl-amino]-propyl}-ethyl-amino)-propyl}-11-desoxy -17R,20S,24,25-tetrahydrofusid-21-amide,
21-N-{3'-({4'-[(3'-amino-propyl)-cyclopropylmethyl-amino]-butyl}-cyclopropylmethyl-amino)-propyl}-17R,20S,24,25-tetrahydrofusid-21-amide, and
21-N-{3'-[(3'-amino-propyl)-(3'-dimethylaminopropyl)-amino]-propyl}-11-desoxy -17R,20S,24,25-tetrahydrofusid-21-amide.

27. A pharmaceutical composition comprising a compound according to any of claims 1-26 together with a pharmaceutically acceptable excipient or vehicle.

28. A composition according to claim 27 comprising another therapeutically active ingredient selected from the group consisting of penicillins, cephalosporins, tetracyclines, rifamycins, erythromycins, lincomycin, clindamycin, flouroquinolones, corticosteroids, hydrocortisone and triamcinolone.

29. The use of a compound according to any of claims 1-26 for the manufacture of a

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medicament for the treatment or prevention of infections.

30. The use according to claim 29, wherein the infection is a bacterial infection.

31. The use according to claim 29, wherein said compound is combined with one or more other therapeutically active ingredients.

32. The use according to claim 31, wherein said therapeutically active ingredient is selected from the group consisting of penicillins, cephalosporins, tetracyclines, rifamycins, erythromycins, lincomycin, clindamycin, flouroquinolones, corticosteroids, hydrocortosone and triamcinolone.

33. A method of preventing or treating infection, the method comprising administering to a patient in need thereof an effective amount of a compound according to any of claims 1-27.

34. A method according to claim 33, wherein said infection is a bacterial infection.

35. A method according to claim 33, wherein said compound is administered simultaneously or sequentially with one or more other therapeutically active ingredients.

36. A method according to claim 35, wherein said other terapeutically active ingredient is selected from the group consisting of penicillins, cephalosporins, tetracyclines, rifamycins, erythromycins, lincomycin, clindamycin, flouroquinolones, corticosteroids, hydrocortisone and triamcinolone.